# 論 文 の 内 容 の 要 旨

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論 文 題 目

Induction of interleukin-10 in the stable transformants of human T-cell line expressing Epstein-Barr virus-encoded small RNAs

（エプスタイン・バーウイルスのコードする小 RNA を安定発現するヒト T 細胞株での インターロイキン 10 発現誘導）

（論文の内容の要旨）


***Background.*** Epstein-Barr virus (EBV) is a ubiquitous virus in humans and latently infects B cells. In some individuals, however, EBV develops chronic active infection (CAEBV) and causes life-threatening complications due probably to cytokinenemia induced by EBV-infected T or natural killer (NK) cells. The *in vitro* infection of human T-cell lines with EBV after the enforced expression of EBV receptor in B-lineage cells, CD21, causes the enhanced production of a macrophage activating cytokine, tumor necrosis factor (TNF)α. However, the responsible EBV gene for the upregulation of TNFα expression in T-lineage cells remains unclear. Profiles of EBV latent gene expression in EBV-infected T and NK cells show variations, and only EBV nuclear antigen-1 and EBV-encoded small non-polyadenylated RNAs (EBERs) are commonly expressed in non-neoplastic infected T and NK cells in CAEBV. EBERs cause interleukin (IL)-10 induction in human B-lineage Burkitt's lymphoma cell lines, however, the role of EBERs in EBV-infected T and NK cells is still unknown.

***Methods.*** The plasmid coding EBERs was introduced into human T lymphocyte virus-I-negative human T-cell lines in a site-directed manner by using Flp recombinase–mediated integration kit Flp-In™ System, and stable transformants were established. The alteration of cytokine expression in EBERs-expressing transformants was examined by real-time RT-PCR analyses. The activation of the downstream signaling cascade from dsRNA were examined by Western blot analyses.

***Results.*** Among three mother T-cell lines and their transformants, only the transformants of MOLT-14 cells (γδ T cells) expressed EBERs. EBERs-expressing MOLT-14 cells produced the larger amount of IL-10 than that from the mother cell line. However, mRNA expression of TNFα, interferon (IFN)γ, and IL-1β in MOLT-14 cells did not affected by EBERs. The phosphorylation of dsRNA-dependent protein kinase (PKR) and that of IκBα□ which act in the downstream of PKR, increased in EBERs-expressing clones.

***Conclusions.*** EBERs did not induce the cytokine with macrophage-activating activities, such as TNFα, IFNγ, and IL-1β. The γδ T cell-specific production of IL-10 through EBERs expression, however, might lead to the modification of function of γδ T cells, and might play a role in human immune diseases.